REDUCTION OF 9-AMINOARYLACRIDINES AND THEIR SALTS

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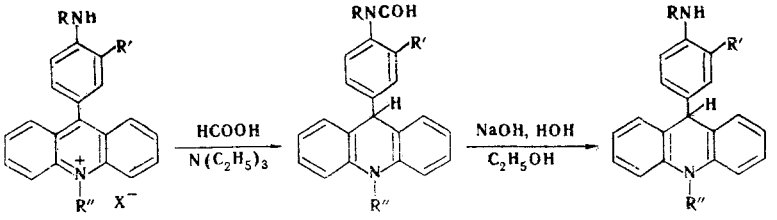
9-Formamidoarylacridans are obtained in the reduction of 9-aminoarylacridines with a free amino group by means of formic acid in the presence of triethylamine. Under these conditions N,N-dialkyl derivatives are cleaved to 9-unsubstituted acridan and dialkylanilines.

9-Aminoarylacridines (I) are obtained smoothly in the reaction of aromatic amines with acridine salts [1]. The present paper is devoted to a study of the reduction of I. The reduction products — acridans — may be of independent interest as antioxidants [2].

Zinc and tin in hydrochloric acid do not reduce I. When hydrazine hydrate is used it adds to the C_9 atom of 9-aminoarylacridine [3]. Positive results were obtained in the reduction with formic acid in the presence of triethylamine. It was found that I with a free amino group behaves differently in this case than dialkylaminoarylacridines. 9-Formamidoarylacridans (IIa-g, Table 1) are formed in the reduction of I having primary and secondary amino groups.



I a-g II a-g IIIa-e, g

a R=R'=R''=H, X=Cl; b R=CH_3, R'=R''=H, X=Cl; c R=R'=H, R''=CH_3, X=I; d R=R''=CH_3, R'=H, X=I; e R=H, R'=R''=CH_3, X=I; f R=H, R'=OH, R''=CH_3, X=I; g R=H, R'=OCH_3, R''=CH_3, X=I

Formic acid in the presence of triethylamine reduces 9-aminoarylacridines and their protic and quaternary salts equally well.

Formylation precedes reduction. For example, the reaction mixture contains primarily 9-formamidophenylacridine (IV) and only traces of starting Ia and reaction products IIa 15 min after the start of reduction of 9-aminophenylacridine (Ia) [according to thin-layer chromatography (TLC)]. 9-Formamidophenylacridan (IIa) is formed in quantitative yield when a genuine sample is refluxed in a mixture of formic acid and triethylamine.

The structure of the acridans obtained was confirmed by spectral methods. The UV spectra of IIa-g contain typical (for acridans [2]) broad absorption bands with λ_{max} 280-290 nm (Table 1). The IR spectra contain characteristic (for secondary amides) "amide I" bands of C=O stretching vibrations at 1660-1680 cm^{-1} and "amide II" N-H deformation vibrations at 1520-1540 cm^{-1}; this indicates the presence of a formamide group.

The formamide group in II is readily saponified by refluxing in aqueous alcoholic alkali. The physical characteristics of the 9-aminoarylacridines (IIIa-e, g) obtained as

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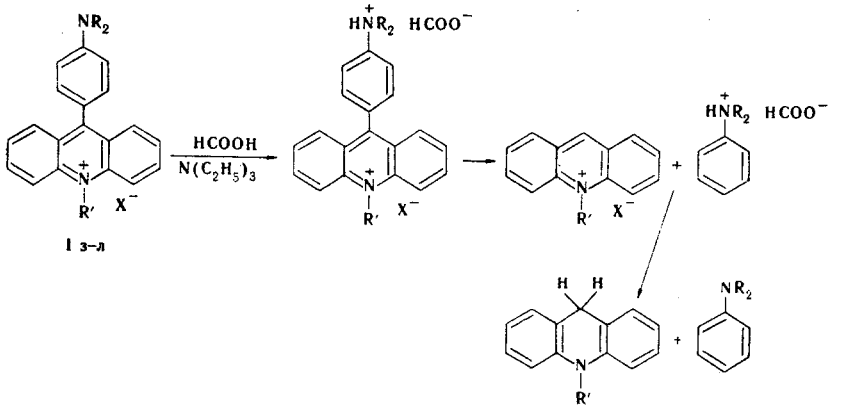
a result of hydrolysis are presented in Table 2. Compounds IIa-g are unstable in air; in the presence of acids they are readily oxidized to the corresponding acridines.

In the reduction of 9-dialkylaminoarylacridines (Ih-k) we observed an interesting phenomenon — cleavage of the C_1-C_9 bond between acridine and dialkylaniline. In this case we obtained 9-substituted acridan (or N-methylacridan) and dialkylaniline in quantitative yields. The dialkylaniline was detected in the reaction mixture by gas — liquid chromatography (GLC).

This cleavage may be due to several reasons. First, it may occur during subsequent reduction of the 9-dialkylaminoarylacridans (V). Second, the cleavage may be due to protonation of V at the para-carbon atom in the arylamine portion of the molecule. For example, 9-phenyl-9,10-dihydroanthracene undergoes decomposition in this way in acidic media [4].

However 9-(4-dimethylaminophenyl)acridan (VI), obtained by alternative synthesis from p-lithiodimethylaniline and acridine [5], does not decompose on reduction with HCOOH and $N(C_2H_5)_3$. The C_1-C_9 bond also is not cleaved by protonation of VI in an argon atmosphere either by formic acid or even by concentrated sulfuric acid.

The reduction of Ih-k in acidic media apparently does not proceed through a step involving the formation of an acridan but via initial reduction of the protonated arylamine portion of the molecule, which bears a positive charge on the nitrogen atom. This also leads to cleavage of the C_1-C_9 bond.



I h R=CH_3, R′=H, X=Cl; i R=C_2H_5, R′=H, X=Cl; j R=R′=CH_3, X=I; k R=C_2H_5, R′=CH_3, X=I

Formyl derivatives of 9-aminoarylacridine, which are incapable of protonation, are reduced in the acridine portion of the molecule to give 9-formamidoarylacridans.

EXPERIMENTAL METHOD

The electronic spectra of alcohol solutions of the compounds were recorded with an SF-4A spectrophotometer. The chromatographic analyses were made with a Vyrukhrom chromatograph with a 4 by 2,000 mm column filled with 20% polyethylene glycol adipate on Celite-545 at 180° with helium as the carrier gas.

The 9-aminoarylacridines and their salts were obtained by the method in [1].

9-Formamidoarylacridans (IIa-g, Table 1). A mixture of 10 mmole of I, 10.1 g (220 mmole) of formic acid, and 4 g (40 mmole) of triethylamine was refluxed for 3 h, after which the mixture was cooled, and the precipitated II (IIa was isolated by precipitation with water) was removed by filtration and crystallized — IIa,b,e, were crystallized from benzene, and IIc,d,f,g were crystallized from alcohol.

9-Aminoarylacridans (IIIa-e,g, Table 2). A 1-mmole sample of II was dissolved in 50 ml of ethanol, 50 ml of 5% aqueous NaOH solution was added, and the mixture was refluxed for 4 h. The precipitated III was removed by filtration and crystallized — IIIa,g were crystallized from ethanol, and IIIb,c,d,e were crystallized from benzene.

TABLE 1. 9-Formamidoarylacridans

Compound	R	R′	R″	mp, °C	Empirical formula	Found, %			Calc.,			UV spectrum	IR spectrum		Yield, %
						C	H	N	C	H	N	λ_{max}, nm (lg ε)	$\nu_{C=O}$	ν_{N-H}	
IIa	H	H	H	217—218	$C_{20}H_{16}N_2O$	79,8	5,4	9,4	80,0	5,4	9,3	235(4,15)	1680	1524	96
IIb	CH_3	H	H	178	$C_{21}H_{18}N_2O$	79,9	5,7	8,9	80,2	5,8	8,9				90
IIc	H	H	CH_3	149—150	$C_{21}H_{18}N_2O$	79,8	5,9	9,2	80,2	5,8	8,9	290(4,17)	1684	1520	93
IId	CH_3	H	CH_3	157	$C_{22}H_{20}N_2O$	80,1	6,3		80,4	6,2		290(4,20)			90
IIe	H	CH_3	CH_3	168	$C_{22}H_{20}N_2O$	80,1	6,4	8,2	80,4	6,2	8,5	290(4,05)	1680	1530	94
IIf	H	OH	CH_3	198—200	$C_{21}H_{18}N_2O_2$	76,0	5,6	8,6	76,3	5,5	8,5	290(4,34)	1661	1534	94
IIg	H	OCH_3	CH_3	200—201	$C_{22}H_{20}N_2O_2$	76,8	5,9	8,0	76,7	5,8	8,1	288(4,38)	1667	1538	99

TABLE 2. 9-Aminoarylacridans

Compound	R	R′	R″	mp, °C	Empirical formula	Found, %			Calc., %			UV spectrum, λ_{max}, nm (log ε)	Yield, %
						C	H	N	C	H	N		
IIIa	H	H	H	184—185	$C_{19}H_{16}N_2$	83,2	6,1	10,2	83,8	5,9	10,3	285(4,18)	95
IIIb	CH_3	H	H	166—167	$C_{20}H_{18}N_2$	83,2	6,3		83,9	6,3			93
IIIc	H	H	CH_3	148—149	$C_{20}H_{18}N_2$	83,7	6,3	10,0	83,9	6,3	9,8	290(4,20)	93
IIId	CH_3	H	CH_3	105	$C_{21}H_{20}N_2$	84,7	6,7		84,0	6,7		285(4,25)	92
IIIe	H	CH_3	CH_3	137	$C_{21}H_{20}N_2$	83,7	6,8	9,5	84,0	6,7	9,3	285(4,26)	81
IIIg	H	OCH_3	CH_3	140—141	$C_{21}H_{20}N_2O$	79,7	6,5	9,1	79,7	6,4	8,8	285(4,40)	90

Reduction of 9-(4-Dimethylaminophenyl)acridine Hydrochloride (Ik). A mixture of 3 g (10 mmole) of Ik, 10.1 g (220 mmole) of formic acid, and 4 g (40 mmole) of triethylamine was refluxed for 3 h, after which it was cooled, and the precipitated 9,10-dihydroacridine was removed by filtration to give a product with mp 172° (from ethanol, mp 172° [2]). Dimethylaniline was detected in the filtrate by GLC. The reduction of Ii,j proceeded similarly.

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